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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/723,180	11/25/2003	Vanda A. Lennon	07039-497001	6610

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EXAMINER	
MERTZ, PREMA MARIA	
ART UNIT	**PAPER NUMBER**
1646	

DATE MAILED: 12/06/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/723,180	LENNON ET AL.	
	Examiner	Art Unit	
	Prema M. Mertz	1646	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *27 October 2005*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-6* is/are pending in the application.

4a) Of the above claim(s) *2 and 4-6* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,2 and 4-6* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *1/11/2005*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Election/Restrictions

1. Applicant's election without traverse of Group I (claims 1-6) in the reply filed on 10/27/2005 is acknowledged.

Claims 7-17 have been canceled in the amendment filed 10/27/2005.

Claims 1-6 are pending and under consideration by the Examiner.

Claim rejections-35 USC § 112, first paragraph, written description

2. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

2a. Claims 1-2, 4-6 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter, which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Claim 1 is drawn to a method of detection by contacting a biological sample with a NMO antigenic polypeptide, wherein said NMO antigenic polypeptide is "aquaporin-4". The claims do not require that the polypeptides of the present invention posses any particular distinguishing feature. Thus, Applicants are claiming a genus of polypeptides that are defined only by sequence similarity.

Vas-Cath Inc. v. Mahurkar, 19USPQ2d 1111, clearly states, "applicant must convey with reasonable clarity to those skilled in the ad that, as of the filing date sought, he or she was in

possession of the invention. The invention is, for purposes of the 'written description' inquiry, whatever is now claimed." (See page 1117) The specification does not "clearly allow persons of ordinary skill in the art to recognize that [he or she] invented what is claimed." (See *Vas-Cath* at 1116). The skilled artisan cannot envision the detailed chemical structure of the encompassed genus of aquaporin-4 polypeptides, and therefore conception is not achieved until reduction to practice has occurred, regardless of the complexity or simplicity of the method of isolation. Adequate written description requires more than a mere statement that it is part of the invention and reference to a potential method of isolating it. The compound itself is required. See *Fiers v. Revel*, 25 USPQ2d 1601 at 1606 (CAFC 1993) and *Amgen Inc. v. Chugai Pharmaceutical Co. Ltd.*, 18 USPQ2d 1016.

One cannot describe what one has not conceived. See *Fiddes v. Baird*, 30 USPQ2d 1481 at 1483. In *Fiddes*, claims directed to mammalian FGF'S were found to be unpatentable due to lack of written description for that broad class. The specification provided only the bovine sequence.

Applicants have only described the human aquaporin-4 polypeptide encoded by the DNA of SEQ ID NO:1. The specification does not provide adequate written description for any polypeptides encoded by a polynucleotide, which deviates from the nucleotide sequence shown in SEQ ID NO:1 (see specification, page 16, lines 3-10). The specification does not describe nucleic acid molecules with 80%, 90%, 95% or even 99% sequence identity with SEQ ID NO:1.

Therefore, only the human aquaporin-4 polypeptides encoded by the nucleic acid set forth in SEQ ID NO:1, but not the full breadth of the claims, meets the written description provision of 35 U.S.C. 112, first paragraph. Applicant is reminded that *Vas-Cath* makes clear

that the written description provision of 35 U.S.C. 112 is severable from its enablement provision (see page 1115).

Claim rejections-35 USC § 112, first paragraph, enablement

2b. Claims 1-2 and 4-6 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a method of detecting the presence or absence of a NMO-specific autoantibody by contacting a biological sample from an individual with a NMO antigenic polypeptide, wherein said NMO antigenic polypeptide is aquaporin-4 and is encoded by a nucleic acid of nucleotide sequence set forth in SEQ ID NO:1; and detecting the presence or absence of binding of said NMO antigenic polypeptide to said NMO-specific autoantibody, wherein the presence of said binding of said NMO antigenic polypeptide to said NMO-specific autoantibody is indicative of NMO in said individual, does not reasonably provide enablement for a method as recited in claim 1. The specification does not enable any person skilled in the ad to which it pertains, or with which it is most nearly connected, to make or use the invention commensurate in scope with these claims.

The factors to be considered when determining if the disclosure satisfies the enablement requirement have been summarized as the quantity of experimentation necessary, the amount of direction or guidance presented, the presence or absence of working examples, the nature of the invention, the state of the prior art, the relative skill of those in the art, the predictability or unpredictability of the art, and the breath of claims. *Ex Parte Forman*, (230 USPQ 546 (Bd. Pat. App. & Int. 1986); *In re Wands*, 858 F.2d 731, 8 USPQ 2d 1400 (Fed. Cir. 1988).

Claim 1 is drawn to a method of detection by using a NMO antigenic polypeptide, said NMO antigenic polypeptide being aquaporin-4. The specification, page 16, lines 4-11, recites:

"A human aquaporin-4 nucleic acid or nucleic acid fragment may have a sequence that deviates from that shown in GenBank Accession Nos. U63622 or U63623. For example, a nucleic acid sequence can have at least 80% sequence identity to the nucleotide sequence shown in GenBank Accession Nos. U63622 and U63623. In some embodiments, the nucleic acid sequence can have at least 85% sequence identity, 90% sequence identity, 95% sequence identity, or at least 99% sequence identity to GenBank Accession Nos. 1763622 and 1763623. See, for example, Genbank Accession Nos. 8C022286, NM 004028, and NM-001650 for variant nucleic acid sequences of aquapolin-4."

While being enabling for using human aquaporin-4 polypeptides encoded by a nucleic acid of nucleotide sequence set forth in SEQ ID NO:1, the specification does not provide enablement for aquaporin-4 polypeptides that are variants to the corresponding wild-type molecules. The specification does not enable any person skilled in the art to which it pertains to make the invention commensurate in scope with these claims. The claims encompass an unreasonable number of inoperative polypeptides, which a person of ordinary skill in the art would not know how to use. Additionally, the claims encompass mutants of aquaporin-4. Therefore, the Applicant's are claiming mutants of aquaporin-4 to be used in the claimed method. The specification does not teach, describe, or provide any examples of mutant aquaporin-4 polypeptides that have been mutated and have at least 80%, 85%, 90%, 95% or 99% sequence identity to the wild-type human aquaporin-4 molecules.

There are no working examples in the specification of an aquaporin-4 polypeptide having less than 100% identity to the wild-type molecule encoded by the nucleic acid set forth in SEQ ID NO:1. A person of ordinary skill in the art would not know how to make aquaporin-4

polypeptides with 99% or less identity to the wild-type sequence. Without a clear delineation of encompassed mutations, a skilled artisan could not know if the mutated aquaporin-4 polypeptides are operable within the present invention. It is well known in the art that single amino acid changes can severely affect polypeptide three-dimensional structure. (Luck et al, Molec. Endocrinol, Vol 5(12), p 1880-1886. In particular, see p. 1881, Table 1). Thus, changes in primary amino acid sequence can affect both tertiary structure and function of polypeptides, and it is not possible for one of ordinary skill in the art to know if the broad claim of the recited aquaporin-4 polypeptides can be used in the instant invention. It would not be predictable to one of ordinary skill in the ad which residues would be critical for polypeptide tertiary structure, and which can be altered and still maintain the characteristics of the protein, therefore a skilled artisan would require undue experimentation in order to use the invention commensurate with the scope of the claims. Furthermore, a skilled artisan would be unable to predict how to mutate aquaporin-4 while still retaining necessary structural without undue experimentation. For these reasons, which include the complexity and unpredictability inherent in the claimed invention and the art, the lack of direction, guidance, or working examples for using aquaporin-4 polypeptides other than those encoded by the nucleic acid set forth in SEQ ID NO:1, and the breadth of the claims, which can essentially encompass mutant aquaporin-4 polypeptides, which could potentially be millions of polypeptides. The Examiner holds that undue experimentation would be required to practice the invention as claimed.

With respect to claim 1 which recites "fragment of said NMO antigenic polypeptide", this which limitation is non-enabled by the specification in the absence of reference to a subset of

amino acid sequences comprising the minimum number of amino acids encompassed by the term "fragment". While the specification, (see page 15, lines 16-18), discloses that:

"As used herein, fragments refer to nucleic acids or polypeptides corresponding to less than the entire aquaporin-4 sequence."

The specification provides no guidance as to which amino acids might comprise the minimum residues of a fragment, which retains the enabled functional property. One would not have a reasonable expectation of successfully making a representative number of fragments having the desired functional activity, consistent with the scope of the claims. Additionally, one would reasonably expect that fragmentation of the aquaporin-4 polypeptide would abolish this desired activity because the minimum number of amino acids required for binding activity is at least 6 amino acids. Furthermore, Harlow et al. teach peptides of six residues in length will consistently elicit antibodies that bind to the original protein (page 76, lines 22-23 in particular). Therefore, in the absence of delimiting amino acid sequences for "fragment" of the polypeptide, a person of ordinary skill in the art would be unable to make fragments of aquaporin-4 embraced by the claims without undue experimentation to determine which fragment has the desired activity.

Conclusion

No claim is allowed.

Claims 1-2, 4-6 are rejected.

Advisory Information

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Prema Mertz whose telephone number is (571) 272-0876. The examiner can normally be reached on Monday-Friday from 7:00AM to 3:30PM (Eastern time).

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Anthony Caputa, can be reached on (571) 272-0829.

Official papers filed by fax should be directed to (571) 273-8300. Faxed draft or informal communications with the examiner should be directed to (571) 273-0876.

Information regarding the status of an application may be obtained from the Patent application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Prema Mertz

Prema Mertz Ph.D., J.D.
Primary Examiner
Art Unit 1646
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